

## CELL SCIENTISTS TO WATCH

# Interview with 2019 Hooke medal winner Eugenia Piddini

Eugenia Piddini studied at the University of Palermo, Italy, before moving to the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, for her PhD on the role of motor proteins in cell shape changes under the supervision of Carlos Dotti. Her postdoctoral work was carried out with Jean-Paul Vincent at the National Institute for Medical Research (now part of the Crick Institute, London). There, Eugenia worked on morphogen gradients during *Drosophila* development and later turned to understanding the mechanisms of cell competition. She became a group leader at the Gurdon Institute, Cambridge, UK, in 2010, to investigate the mechanisms of cell competition in homeostasis and in a tumour–host-cell context. In 2016, Eugenia moved to the University of Bristol, UK, as a Senior Research Fellow and was appointed Professor one year later. She is the recipient of the 2019 Hooke medal, established to recognize an emerging leader in cell biology. The Hooke medal is awarded at the annual spring meeting of the British Society for Cell Biology (BSCB).



Eugenia Piddini

### What inspired you to become a scientist?

As a child, I was fascinated by different things, many science-related. I dreamt of being an archaeologist because I liked the discovery aspect. But when I was in high school, I became passionate about genetic engineering – or the bits I could understand about it at that time. I was amazed by the idea of making square tomatoes so they would fit better in boxes, things like that. This led me to wanting to understand of how cells work and how we can use that for health and societal benefits.

### Sicily is a good place to grow up if you're interested in archaeology

In fact, my parents had a summer house right by the sea on top of a hill, which was formed of sandstone. Embedded in the sandstone, when you started digging, there were these very beautiful marine creatures, shells and other hidden things. I enjoyed going there as a child to dig and find these fossils and remains.

### How did you decide to do your PhD at the EMBL in Heidelberg?

I had a really strong desire to leave Italy and experience science abroad, and the EMBL was one of those locations that I dreamt of because it looked fantastic and I wanted to be there. My training was in cell biology and I travelled across certain organelles, so to speak – from mitochondria via the ER to the cytoskeleton; a good voyage inside the cell. At the end of my PhD and for my postdoc, it became central to me to address how the inner workings of a cell become important for the surrounding cells, or cells within a community.

### The beginning of your passion for cell competition and its mechanisms

Yes and I think the field of cell competition is really at its prime today. It has only been a few years since it was established and accepted that cell competition is happening across species – for a long time, it was

considered a *Drosophila*-only phenomenon – and across tissues as well, from development to adulthood. So it is becoming increasingly clear that it is a fundamental biological phenomenon that can have massive implications for health and disease.

### What questions related to cell competition are you trying to answer in your research group?

We try to understand the role that cell competition plays in cancer, and for that we use both *Drosophila* and mammalian cell culture models. We are also interested in the physiological contexts in which cell competition may be happening. As an example, in a recent project, we are investigating whether cell competition plays a role in wound closure, and we have evidence that indeed some cells that are involved in wound healing are cleared at the end of the process by cell competition, using pathways that we have previously identified in the lab. In general, the broad question we are trying to address is what is it that is different about the cells that are eliminated by competition when they are no longer so fit? We are looking at cellular defects and trying to understand which of these defects turns them into, so to speak, 'losers'. 'Loser' is the definition we give to cells which are eliminated when a fitter cell population is present.

### The cell competition choice to lose a cell can be beneficial or deleterious to the organism – how does this come about?

It is a great example of a biological process that has evolved to the benefit of the organism but that can be exploited in pathological conditions like cancer. A tissue that is made of a multitude of cells, which need to live as a community for quite a long time, benefits from quality control; if cells accumulate damage or start behaving aberrantly, it is beneficial in some ways if you have a sentient mechanism that recognises these cells and cleans the tissue of them. This would therefore be one of the main functions of cell competition – to remove compromised or mis-specified cells. Furthermore, in adult tissues, the first cells that accumulate neoplastic mutations may be recognised and eliminated by competition. This happens in a number of contexts and you can see how this mechanism might be hijacked by a cell when it manages to persuade their neighbours that they're fitter and how this might become a problem for the organism.

Eugenia Piddini's contact details: Biomedical Sciences Building, University of Bristol, Tankard's CI, University Walk, Bristol BS8 1TD, UK.  
E-mail: ep16996@bristol.ac.uk



Eugenia with her 8-month-old daughter Giulietta.

### What would be an example of this hijacking?

One observation goes back to my postdoc in Jean-Paul's lab; during fly development, cells with reduced Wnt pathway signalling activity are eliminated through cell competition as a means to clear mis-specified cells. At the time we also showed that overactivation of the Wnt pathway can result in these cells killing cells that are wild type. The Wnt pathway is overactivated in a number of cancers, particularly in intestinal tumours where a mutation in the adenomatous polyposis coli (*APC*) gene – a negative regulator of the Wnt pathway – is an early event in tumorigenesis. This led us to hypothesize that cell competition might play a role in the establishment of these tumours. More recently in my group, using an APC-driven *Drosophila* intestinal cancer model, we have shown that tumour cells with mutations in APC kill surrounding host cells and, if we prevent their ability to kill, they can no longer expand and form intestinal tumours. Thus, in this context, cell competition is hijacked by cancer cells and becomes a driver of tumorigenesis.

### How are these processes controlled through mechanical interactions and their influence on cellular signalling?

There is accepted evidence now that cells have multiple ways to compete. They may do so through specific ligand–receptor interactions or differences in sensitivity to their mechanical environment. We were able to identify the tumour suppressor p53 as a key sensor for cell competition and mechanical stress. Every cell finds itself in a physical environment and needs to integrate physical information with (bio)chemical information. Therefore, having a general pathway like p53 that is also a node for stress signalling convergence, seems to me like a very evolved, adaptive way to be able to translate stress signalling into mechanical sensitivity. It allows cells that are stressed to be eliminated if they are surrounded by non-stressed neighbours.

### You mentioned that you see the cell competition field is at its prime. Did you anticipate this earlier in your career?

No, I didn't. It is true that we are not trained to think that way; once you have more experience and a better appreciation for what happens in science around us, it is clear that there are questions that come of age or will be in demand. I was just very lucky; it was a bit serendipitous that I became interested in competition, because it was not something my postdoc lab was working on and we stumbled over it. I was absolutely fascinated by it so I decided to continue working on it and it was a phenomenon that we knew relatively little about, so it was a perfect fertile ground that you want to start on for your independence, and it turned out to be the right strategic decision.

### Having a strategy is therefore important advice you would give to someone seeking independence?

Senior researchers may have a bit of perspective on the fields and can advise you on what would be a good or a bad choice for an area to be working in. I believe there are three things that are really important in helping to make a scientist successful. One is the research area, but there are also the model system that one uses and technologies and method development that are really transformative. The combination of a good question, a powerful model system and a transformative technology is an ideal recipe to start an independent career.

Regarding the model system – research in *Drosophila* has, again, proven how powerful 'classic' model systems are.

This is a really important point, also in terms of thinking strategically: how does one go about answering scientific questions? For me, it is about finding the best system to address a question – if you do that, then it takes care of whether a model system is 'hot' or not. It is unjustified to shut down a model system because of its age, much as it is unjustified to stick to one system because your career was built on that and you're trying to answer any and all questions on that system. Try to be smart about which model system is best suited to answer a specific question. We started as a *Drosophila* and mammalian cell culture lab; my first postdoc was experienced with flies and the second and third were trained in mammalian cell culture. I thought this was going to be important to allow us to progress and it turned out we were possibly the first lab to combine both systems to work on cell competition.

**“The combination of a good question, a powerful model system and a transformative technology is an ideal recipe to start an independent career.”**

### What characteristics do you look for when recruiting new group members?

Who you recruit for your lab absolutely defines how successful you will be. I believe that you can only be as good as the people that you have in your group and I find it essential to recruit scientists that are very excited and driven by the discovery process and are in it because they really enjoy research. Then, working in the lab becomes a blast and having motivated people helps to form a community within your group – it becomes an exciting environment that makes things happen. Unfortunately, when it comes to recruitment, I and many colleagues are currently experiencing the 'Brexiteffect', which is not sending a very positive, friendly and welcoming message to international applicants from Europe and all

around the world. This is something that comes up all the time when I am at conferences talking to students and postdocs.

**Do you discuss careers outside academia with your students?**

Yes, because I think that we shouldn't be training a generation of unemployed people. Only a few percent of PhD students will go on to become a group leader. What are we going to do, be oblivious to this? Academic research is but one of many career prospects and many are just as exciting. After my PhD, I seriously considered going into consulting. I wanted to do an MBA and move into consulting for venture capitals and I found that incredibly exciting. Had I embraced a career in consulting, I am sure I would have been just as fulfilled and excited as I am now. With that in mind, to me it has never been about 'alternative' careers; it's been about you and your vocation and where your interests take you once you've done a PhD.

**“...you can only be as good as the people that you have in your group...”****Is this part of your advice to students and postdocs working with you?**

I first want to know what they want to do in their career. Then, I want to make sure they made that decision because they think it is best for them and not because they think that this is all they can achieve. Two of my postdoc alumni have stayed in academia and two left academia to go into the private sector. They were both convinced that this is what they wanted and they are satisfied with their decision.

**How do you get the most out of the meetings you attend, particularly in the early stages of your career?**

Conferences are one of the most exciting things we get to do as scientists. I like to combine the unmissable, topical conferences with the ones that have a much bigger breadth and areas that are not exactly spot on with what one does. For the latter, I just sit back and enjoy the show having all these talks parading and enjoy being impressed by the next discovery I wasn't expecting. I find it very inspiring. With regards to presenting your data, especially early in your career, I feel that what makes a talk successful is disclosing unpublished information because this is what will open up the possibility of collaborations, or someone will come to see you and tell you 'I think you should be looking at x because this is what we have seen etc.'. It is from these interactions that progress sparks.

**Could you tell us an interesting fact about yourself that people would like to find out about you?**

We talked about Sicily at the beginning and that's where I also would like to finish! I'd like to highlight that I am a proud Sicilian. Even though I left home 21 years ago, I still feel every bit Sicilian as I did then and I am very proud of my origins and my heritage. It has shaped who I am in countless ways – the warmth of the people, their passion for life, family values and their communication. I think this all permeates who I am, as well as how I do science.

Eugenia Piddini was interviewed by Manuel Breuer, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.